## REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

Claims 6, 8-17, and 22-24 are drawn to non-elected groups. As such, Applicants request that Claims 6, 8-17, and 22-24 be withdrawn from consideration. However, Applicants reserve the right to pursue these claims on the merits in a continuation or divisional application, or to request that these claims be rejoined in the instant application.

Claims 1, 5, and 7 are currently being amended.

Claims 25-29 are being added.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, are presented, with an appropriate defined status identifier.

After amending the claims as set forth above, Claims 1-5, 7, 18-21, and 25-29 are now under consideration in this application.

Applicants note that an information disclosure statement was filed on February 7, 2002. Applicants respectfully request that the information disclosure statement be acknowledged.

In the Office Action dated February 26, 2003, the Examiner objected to Claim 7 for reciting the term "antobody." Applicants have corrected this typographical error, and amended Claim 7 recites "antibody." Applicants request that the Examiner withdraw the objection.

In the Office Action, the Examiner also rejected Claims 2 and 4 under 35 U.S.C. § 112, second paragraph, for using the terms "anti-NCA-90" and "anti-NCA-95" which contain an abbreviation of an antigen name (*i.e.*, non-specific cross-reactive antigen). (Applicants note that the limitations of Claims 2 and 4 have been incorporated in Claim 1.) Applicants respectfully traverse the rejection because the terms "anti-NCA-90" and "anti-NCA-95" are readily recognized by those skilled in the art of anti-granulocyte antibodies as referring to antibodies against the 90 kD and the 95 kD non-specific cross-reacting antigens of granulocytes. Those skilled in the art typically use the acronym "NCA" rather than the term "non-specific cross-reacting antigen" because the term "non-specific cross-reacting antigen" is long and awkward. As such, one skilled in the art of anti-granulocyte antibodies would recognize the metes and bounds of the claims, and Applicants respectfully request that the Examiner reconsider the rejection under 35 U.S.C. § 112, second paragraph.

In the Office Action, the Examiner also rejected Claims 3, 5, and 20 under 35 U.S.C. § 112, first paragraph, for failing to satisfy the written description requirement. The Examiner contends that Claims 3, 5, and 20 recite antibodies that are not "known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public." Applicants respectfully traverse the rejection because the recited antibodies are known and obtainable, or otherwise readily available to the public.

Claim 3 recites "MN-3." MN-3 belongs to a class of antibodies that have been shown to react with epitope I of the carcinoembryonic antigen. *See* Jessup, *et al.*, *Int. J. Cancer*,

Sep. 9;55(2):262-8 (1993). The specification describes how MN-3 was isolated and characterized. *See* specification at page 9, lines 17-24 (citing Hansen *et al.*, *Cancer* 71:3478-3485 (1993); Becker *et al.*, *Semin. Nucl. Med.* 24(2):142-53 (1994); and Watt *et al.*, *Blood* 78:63-74 (1991)). As such, following the teachings in the specification, one skilled in the art of antibody production could readily produce monoclonal antibodies to epitope I to obtain antibodies that demonstrate the physiological and biological characteristics of MN-3 without undue experimentation. Further, MN-3 reacts with NCA-90, and a listing of some reported anti-NCA-90 antibodies is provided at:

**http://www.mh-hannover.de/aktuelles/projekte/hlda7/hldabase/CD66c.htm**.

Claim 5 recites "MN-3, MN-15, NP-1, MN-2, and NP-2." MN-3 is discussed above. MN-15 and NP-1 are class I anti-CEA antibodies, and MN-15 and NP-1 have been shown to react with epitope II of the carcinoembryonic antigen. *See* Jessup, *et al.*, *Int. J. Cancer*, Sep. 9;55(2):262-8 (1993). The specification describes how MN-15 and NP-1 were isolated and characterized. *See* specification at page 10, lines 4-9 (citing Hansen *et al.*, *Cancer* 71:3478-3485 (1993), lines 17-23 (citing *Krupey et al.*, *Immunochem.*, 9:617 (1972); Newman *et al.*, *Cancer Res.*, 34:2125 (1974); Primus *et al.*, *Cancer Res.*, 43:686-92 (1983); and U.S. Patent No. 4,818,709). As such, one skilled in the art of antibody production could readily produce monoclonal antibodies to epitope II to obtain antibodies that demonstrate the physiological and biological characteristics of MN-15 and NP-1 without undue experimentation. Further, MN-15 and NP-1 cross-react with NCA-90 and NCA-95. A citation for a listing of anti-NCA-90 antibodies is provided above, and a listing of anti-NCA-95 antibodies is provided at:

**http://www.mh-hannover.de/aktuelles/projekte/hlda7/hldabase/CD66b.htm**;

MN-2 and NP-2 are class IIA anti-CEA antibodies, and the specification describes how MN-2 and NP-2 were isolated and characterized. *See* specification at page 9, lines 29-32, (citing Hansen, *et al.*, *Cancer* Jun. 1; 71(11):3478-85 (1993)); page 10, lines 1-3 (citing U.S. Patent No. 4,818,709, which is incorporated by reference); and page 10, lines 10-16 (citing *Krupey et al.*, *Immunochem.*, 9:617 (1972); Newman *et al.*, *Cancer Res.*, 34:2125 (1974); Primus *et al.*, *Cancer Res.*, 43:686-92 (1983); and U.S. Patent No. 4,818,709). Further, U.S. 4,818,709, which is incorporated by reference, teaches how MN-2 and NP-2 can be made, and characterized. For instance, NP-2 reacts with CEA and MA. NP-2 binding to CEA is blocked by NP-1, but NP-2 does not react with NCA, now known as NCA-50/90 (CD66e). Another property that can be used to select MN-2 and NP-2 is that they react with granulocytes in frozen sections, but they do not react with granulocytes in conventional formalin-fixed, paraffin embedded tissues. *See* Hansen, *et al.*, *Cancer* Jun. 1; 71(11):3478-85 (1993). As such, one skilled in the art of antibody production could readily produce and isolate antibodies that demonstrate the physiological and biological activity of MN-2 and NP-2 without undue experimentation.

Finally, Claim 20 recites "M-195," which is deposited with the ATCC under accession number HB 10306 and is readily obtainable for a fee.

Therefore, because all the recited antibodies are known and obtainable, or otherwise readily available to the public, Applicants respectfully request that the Examiner reconsider the rejection 20 under 35 U.S.C. § 112, first paragraph.

In the Office Action, the Examiner rejected Claims 1-5, 7, and 18-21 under 35 U.S.C. § 112, first paragraph, stating that "[t]he specification does not enable any person skilled in

the art to which it pertains, or with which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims." The Examiner contends that the specification teaches the administration of hMN3 and co-administration of hMN3 and anti-CD33, but "nowhere in the specification does it teach the use of any and all types of anti-granulocyte antibodies, nor does it teach the administration of any NCA-95 antibodies for the treatment of CML." The Examiner also contends that "the specification has not taught how to administer two granulocyte antibodies for the treatment of CML." Finally, the Examiner states that "considering [the] large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim." Applicants traverse the rejection for the reasons stated below.

First, Applicants note that Claim 1 has been amended and does not recite "the use of any and all types of anti-granulocyte antibodies." Rather, Claim 1 recites "wherein said anti-granulocyte antibody is an anti-NCA-90 antibody or an anti NCA-95 antibody." In support of the claim, the specification discloses the treatment of CML by administering an anti-NCA-90 antibody, (*see* specification at page 25, Example 1), and the treatment of CML by administering an anti-NCA-90 antibody and an anti-CD33 antibody (*see* specification at page 26, Example 2). Further, the specification provides suggested dosages and modes of administration, (*see* specification at page 22, lines 17-32 and page 23, lines 1-10).

Second, Applicants note that any method of treating CML will require some experimentation, regardless of how sufficiently the method is disclosed. As noted in the specification and as recognized by one skilled in the art of immunotherapy, "the dosage of administered naked anti-granulocyte antibodies...will vary depending upon such factors as

the patient's age, weight, height, sex, general medical condition, disease state and previous medical history." *See* specification at page 22, lines 17-20. As such, a successful method of treatment of CML must be determined empirically and will involve some experimentation. However, "[t]he test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." MPEP § 2164.01 (citing In re Angstadt, 537 F.2d 498, 504 (C.C.P.A. 1976) (emphasis added)). Because of the nature of the claimed subject matter, some experimentation is necessary, but Applicants contend that such experimentation is not "undue."

Third, the state of the art of immunotherapy is advanced, and the level of one of ordinary skill is high. In reading the specification, one of ordinary skill could empirically develop a successful CML treatment regimen for an individual patient that maximizes the therapeutic value of the treatment while minimizing side effects. Further, as stated in MPEP § 2164.01(c), "it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation" (emphasis added). Nonetheless, as noted above, the specification does provide suggested dosages and modes of administration.

Although the Examiner contends that the specification does not "teach the administration of any NCA-95 antibodies for the treatment of CML," Applicants note that because of a high degree of sequence homology between NCA-90 and NCA-95, a number of Mabs against NCA-90 will cross react with NCA-95 (*e.g.*, MN-15 and NP-1, *see* specification at page 10, lines 4-9 and lines 17-23). Further, "[i]f one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be

sufficient to satisfy 35 U.S.C. § 112, first paragraph." MPEP § 2164.01(c) (emphasis added). As such, for the foregoing reasons, Applicants respectfully contend that amended Claim 1, Claim 2, and Claim 4 are enabled. Likewise, because MN-3, MN-2, MN-15, NP-1, and NP-2 demonstrate similar physiological or biological activity, Applicants respectfully contend that amended Claims 3 and 5 are enabled. In regard to amended Claim 7 and new Claim 25, the specification discloses methods for producing a "subhuman primate antibody, murine monoclonal antibody, chimeric antibody, humanized antibody and human antibody," (*see* specification page 11, lines 4-32; and page 12, lines 1-7). As such, Applicants respectfully contend that Claim 7 and new Claim 25 are enabled. In regard to Claim 18 and new Claim 26, Applicants note that CD33 is expressed on granulocytes, and as such, anti-CD33 is an anti-granulocyte antibody. Therefore, Applicants respectfully contend that Claim 18 and new Claim 26, which recite "two or more naked anti-granulocyte antibodies," are fully enabled. In regard to Claims 19-20 and new Claims 27-28, Applicants note that a method of administering anti-CD33 is disclosed, and Applicants respectfully contend that Claims 19-20 and new Claims 27-28 are enabled. Finally, Applicants note that anti-CD33 antibodies and anti-CD15 antibodies demonstrate similar physiological or biological activity, and as such, Applicants respectfully contend that Claim 21 and new Claim 29 are enabled. For all these reasons, Applicants respectfully request that the Examiner reconsider the rejection under 35 U.S.C. § 112, first paragraph.

In the Office Action, the Examiner rejected Claims 1, 5, and 7 under 35 U.S.C. § 102(b) as being anticipated by Seybold. Applicants respectfully traverse the rejection because Claims 1, 5, and 7 recite administering a therapeutic composition that includes "at least one

naked anti-granulocyte antibody." In contrast, Seybold discloses the use of Mab 47 labeled with $^{123}I$, and as such, Seybold does not disclose a naked anti-granulocyte antibody. Seybold does not teach all the limitations of the rejected claims, and therefore, Applicants respectfully request that the Examiner reconsider the rejection under 35 U.S.C. § 102(b).

In the Office Action, the Examiner rejected Claims 1 and 7 under 35 U.S.C. § 102(b) as being anticipated by Caron *et al.* Applicants respectfully traverse the rejection because Caron *et al.* does not disclose an "anti-NCA-90" antibody or an "anti-NCA-95" antibody as recited in amended Claim 1. Rather, Caron *et al.* discloses an anti-CD33 antibody. Because Caron *et al.* does not teach all the limitations of the rejected claims, Applicants respectfully request that the Examiner reconsider the rejection under 35 U.S.C. § 102(b).

In the Office Action, the Examiner rejected Claims 1, 7, 18, and 21 under 35 U.S.C. § 102(a) as being anticipated by Thomas *et al.* Applicants respectfully traverse the rejection because Thomas *et al.* does not disclose "administering to said patient a therapeutic composition." Rather, Thomas *et al.* teaches an antibody composition for processing a blood or bone marrow sample taken from a CML patient. Therefore, Thomas *et al.* does not teach the recited method, and Applicants respectfully request that the Examiner reconsider the rejection under 35 U.S.C. § 102(a).

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 5/22/03 By M. Scott McBride

FOLEY & LARDNER
777 E. Wisconsin Avenue
Milwaukee, WI 53202
Telephone: (414) 297-5529
Facsimile: (414) 297-4900

M. Scott McBride
Attorney for Applicants
Registration No. 52,008